Supplemental material

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BMJ Open Diab Res Care

Molecular and pharmacological characterization of insulin icodec: a new basal insulin analog designed for once-weekly dosing

Erica Nishimura, Lone Pridal, Tine Glendorf, Bo Falk Hansen, František Hubálek, Thomas Kjeldsen, Niels Rode Kristensen, Anne Lützen, Karsten Lyby, Peter Madsen, Thomas Åskov Pedersen, Rasmus Ribel-Madsen, Carsten Enggaard Stidsen, Hanne Haahr

Online supplemental material

Supplemental Figure 1 – Trial design and methodology of the clinical pharmacology trial.
(A) Overall trial design. (B) Methodology during week 5 of treatment in each cohort. OD,
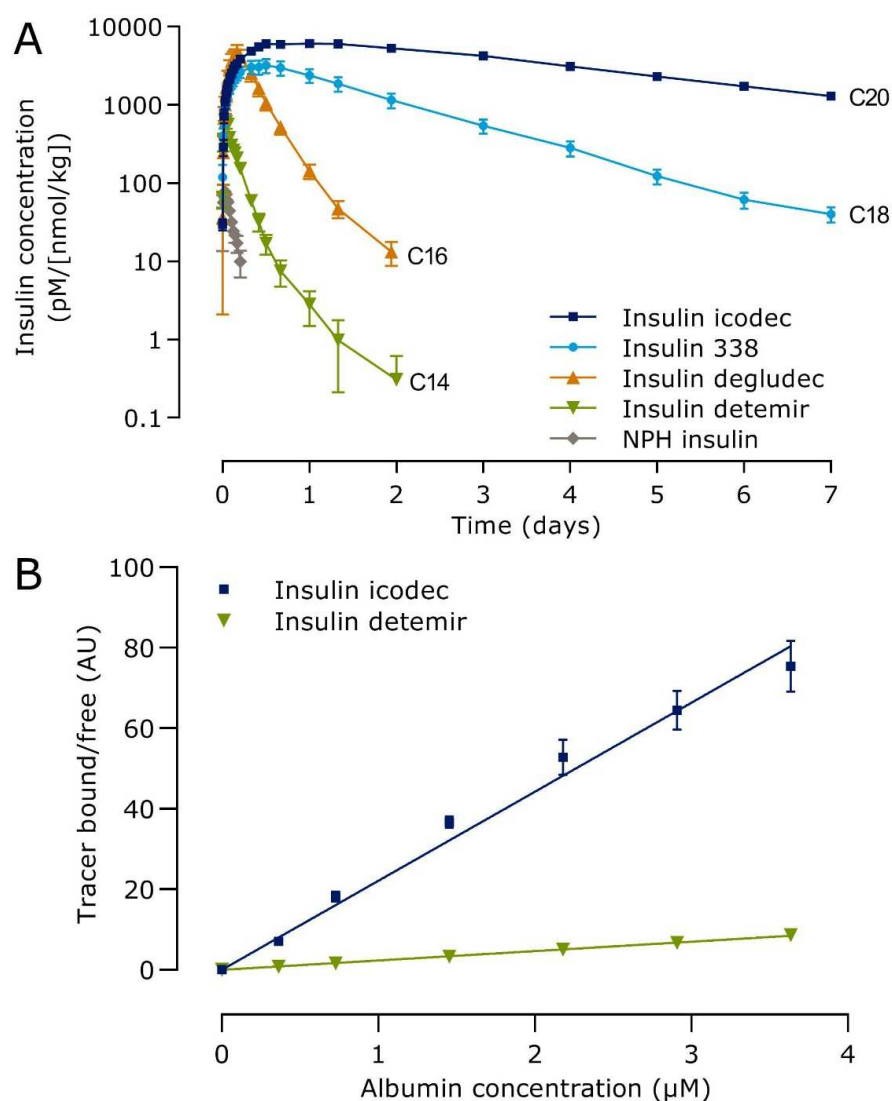once daily; OW, once weekly; U, units.
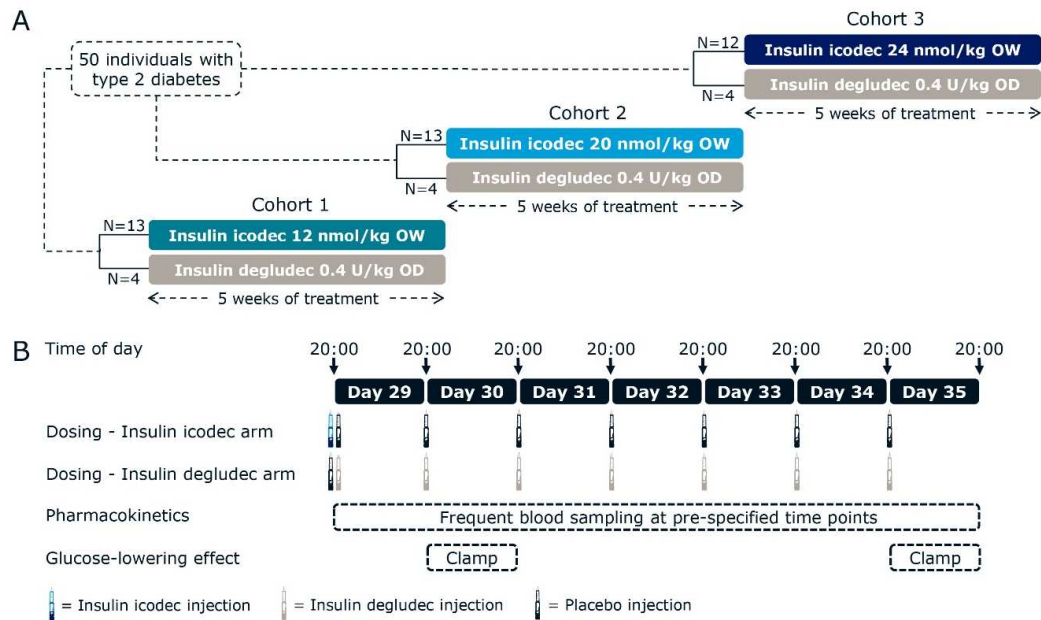
Supplemental Table 1 – Blood sampling for pharmacokinetic analysis of insulin icodec in the clinical pharmacology trial

Day	Nominal time[a] (hours)	Insulin icodec	Day	Nominal time[a] (hours)	Insulin icodec
1	00[b]	X		12	X
	01	X		16	X
	02	X		20	X
2	04	X		24	X
	06	X		26	X
	10	X	31	28	X
	14	X		30	X
	16	X		32	X
	18	X		34	X
	20	X		36	X
	24	X		40	X
3	30	X		44	X
	36	X		48	X
	42	X	32	60	X
	48	X		72	X
4	60	X	33	84	X
	72	X		96	X
5	84	X	34	108	X
	96	X		120	X
6	108	X	35	132	X
	120	X		144	X
7	132	X		146	X
	144	X	36	148	X
8	156	X		150	X
	00[b]	X		152	X
9	12	X		154	X
	24	X		156	X
15	00[b]	X		160	X
16	12	X		164	X
	24	X		168	X
22	00[b]	X	39	228	X
23	12	X	44	348	X
	24	X	51	516	X
29	00[b]	X	65	852	X
30	06	X			

[a] Relative to last insulin icodec dose at 20:00 hours; [b] Pre-dose.

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Supplemental Figure 2 – (A) Pharmacokinetic profiles of various insulin molecules after a single subcutaneous dose in dogs. C14, C16, C18 and C20 refer to the carbon length of the fatty acid side chains used in the different insulin analogs (n=6 for insulin icodec, 338, degludec and detemir and n=5 for NPH insulin). Error bars show standard error of the mean. (B) Albumin binding of insulin icodec in comparison to insulin detemir (n=3). Error bars show standard error of the mean. Lines show the non-linear fit. AU, arbitrary units; NPH, neutral protamine Hagedorn.

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Supplemental Table 2 – Baseline characteristics in the clinical pharmacology trial

	12 nmol/kg cohort	20 nmol/kg cohort	24 nmol/kg cohort
Number of individuals with type 2 diabetes	13	13	12
Age, years	57.5±4.9	58.1±4.6	57.8±3.3
Males, n (%)	11 (84.6)	11 (84.6)	11 (91.7)
Body weight, kg	93.6±13.5	94.1±14.3	93.9±13.1
BMI, kg/m^2	29.6±3.2	30.3±3.0	29.8±2.3
HbA$_{1c}$, %	7.4±0.6	7.5±0.7	7.2±0.7
Diabetes duration, years	14.8±5.1	15.3±9.0	13.0±5.7
Metformin at screening, n (%)	0 (0.0)	0 (0.0)	7 (58.3)

Insulin icodec once-weekly doses correspond to 0.29, 0.48, 0.57 U/kg/day anticipating equipotency to once-daily basal insulins. Data are mean±standard deviation unless otherwise stated. HbA$_{1c}$, glycosylated hemoglobin; BMI, body mass index; U, units.